THE 2nd PERINATAL MEDICINE SCIENTIFIC RESEARCH AWARD

OLFM4 Polymorphisms with Severe Outcomes in Preterm Neonates With Sepsis

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OUTLINE

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1. BACKGROUND

What's already known?

- Sepsis: leading cause of death in preterm infants. Early risk identification is critical.
- Neutrophils: central roles in the innate immune response
- **Olfactomedin 4 (OLFM4)** marks **two** distinct neutrophil populations: OLFM4**+** (10-30%) and OLFM4**–**
- *OLFM4* gene upregulated in infection, with variants linked to septic shock outcomes in adults.

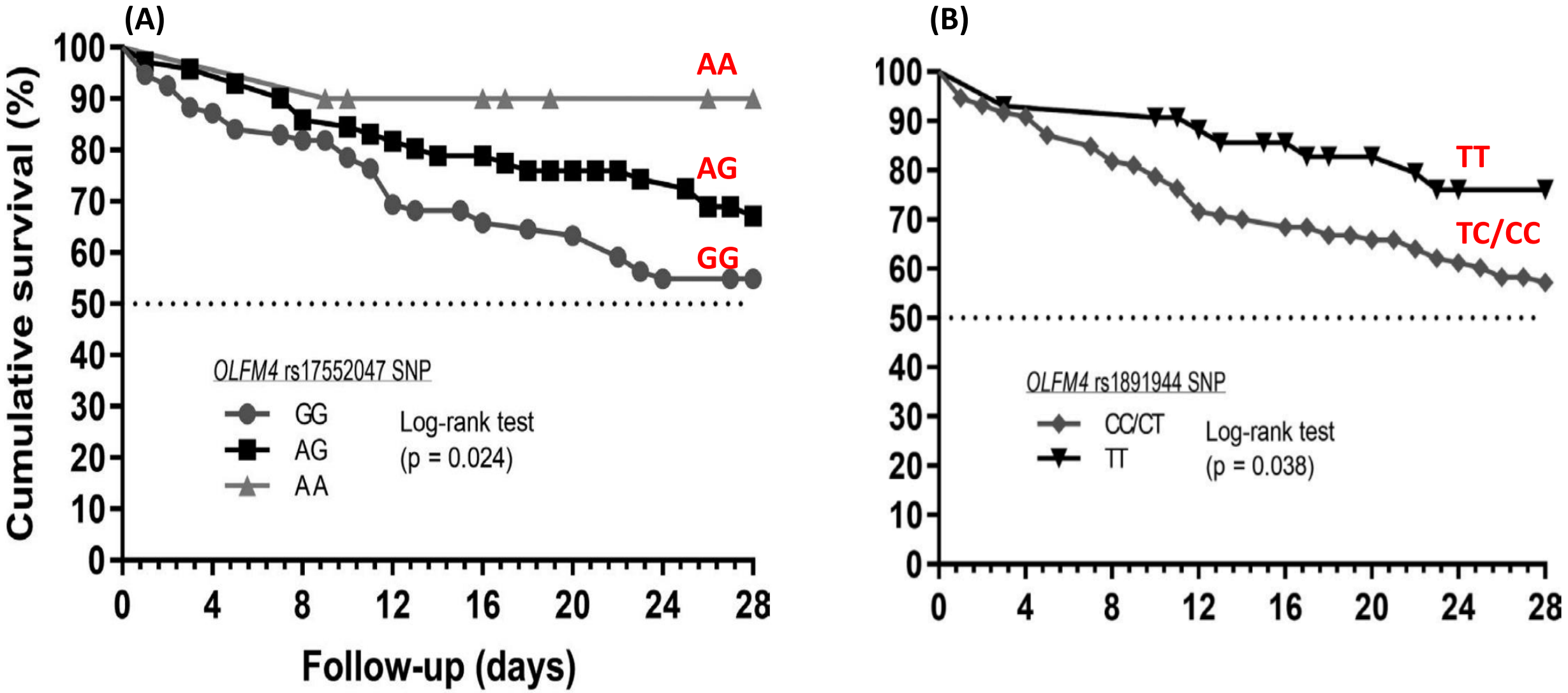


Figure 1. Survival analysis in adults with septic shock by genotypes at rs17552047, rs1891944

Source: Pérez-García F, Resino S, Gómez-Sánchez E, et al. OLFM4 polymorphisms predict septic shock survival after major surgery. *Eur J Clin Invest*. 2020;51(4):e13416

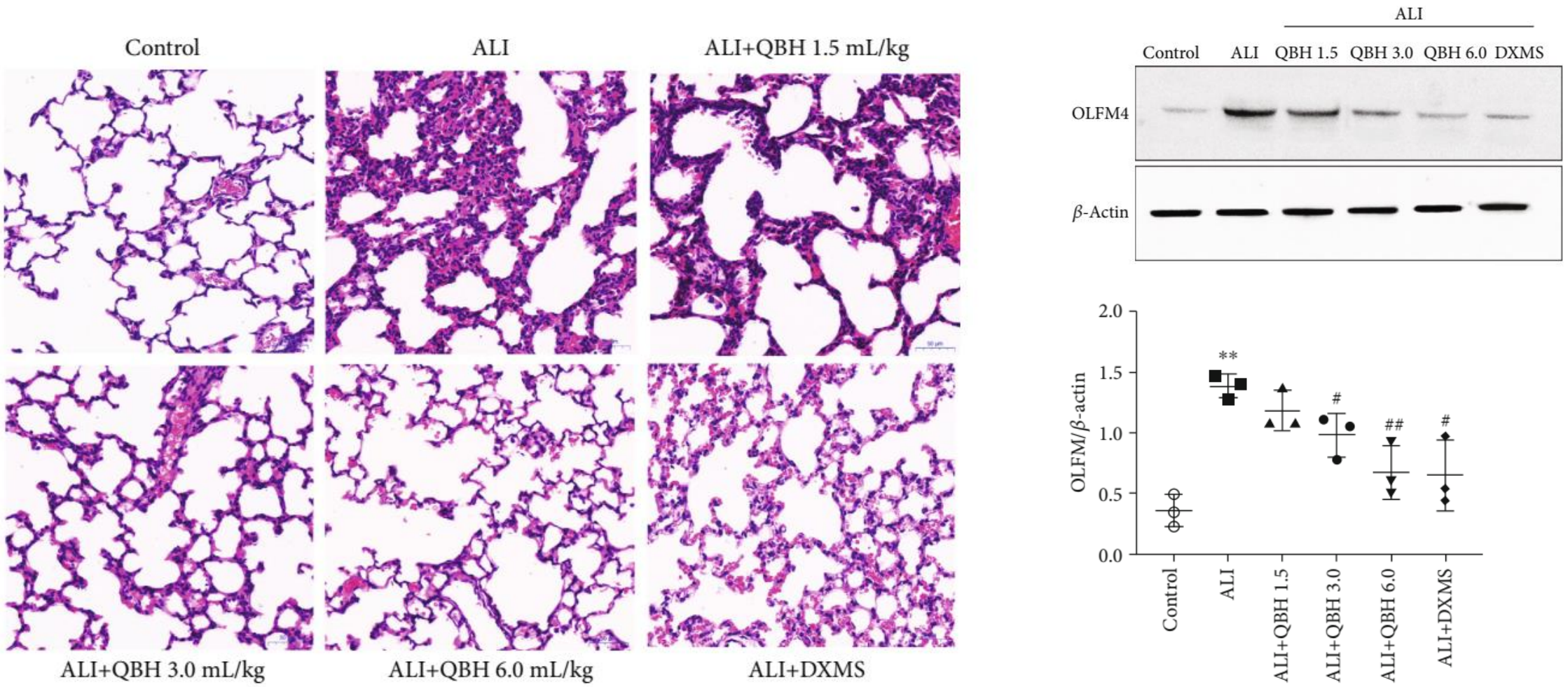


Figure 2. QBH protects against sepsis-induced ARDS by inhibiting *OLFM4*

Source: Zhang F, Li Y, Xi Y, et al. Qinbaohong Zhike Oral Liquid Attenuates LPS-Induced Acute Lung Injury in Immature Rats by Inhibiting OLFM4. *Oxid Med Cell Longev*. 2022;2022:7272371

What this study adds?

- Moves toward **precision medicine** in neonatal sepsis through genetic stratification.
- Enables **early risk prediction** using *OLFM4* genotypes in preterm infants.
- Lays groundwork for **personalized management** and future **targeted therapies**.

2. OBJECTIVES

Research question:

Are the **genotypes** at rs17552047 and rs1891944 of *OLFM4* gene

associated with **severe outcomes**

in **neonatal sepsis** among preterm infants?

Hypothesis:

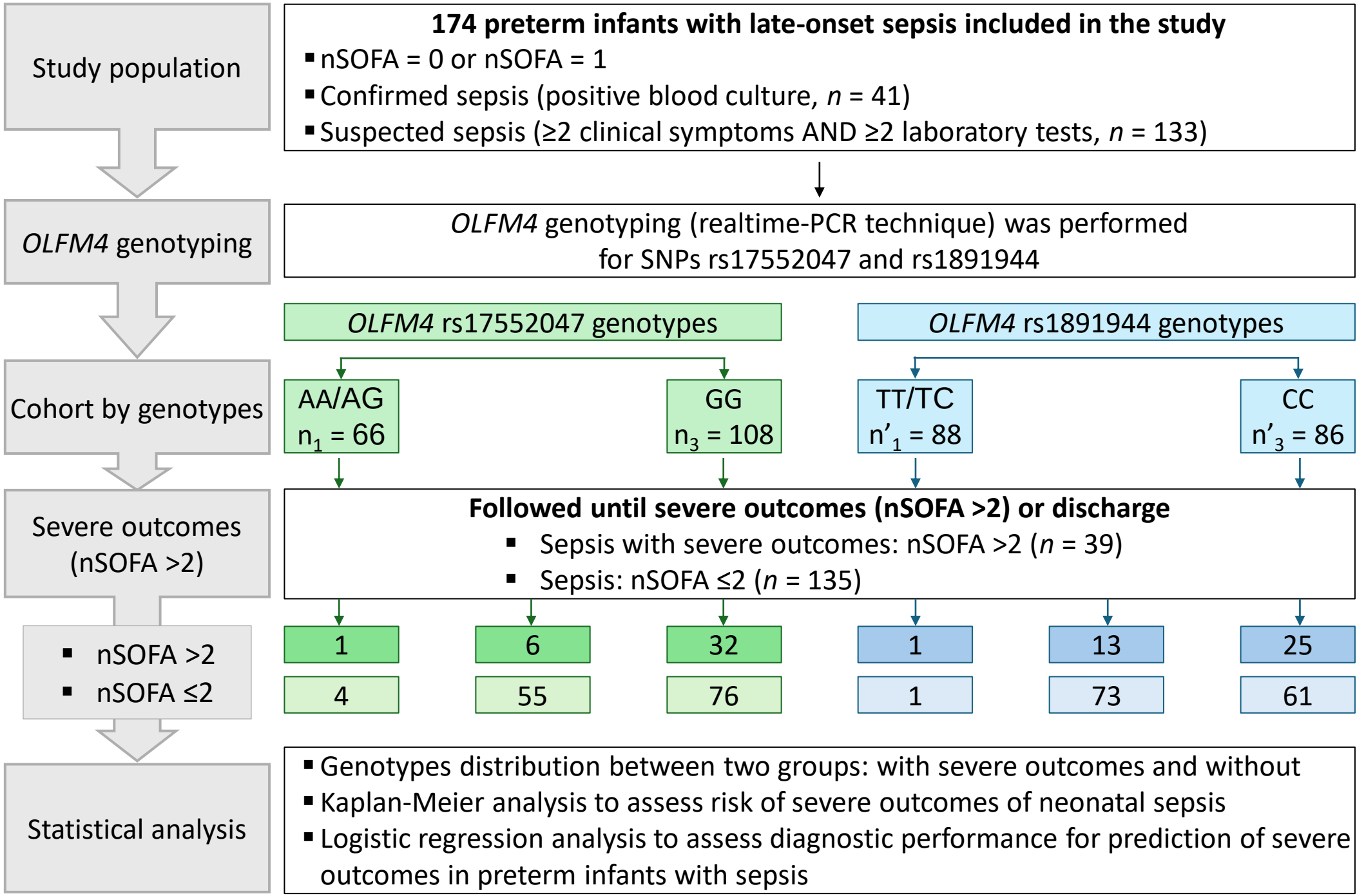
We hypothesize that the presence of the **A allele at rs17552047** and the **T allele at rs1891944** of the *OLFM4* gene associated with a **reduced risk of severe outcomes** in neonatal sepsis among preterm infants.

Objectives:

1. To determine the association between rs17552047 A allele and rs1891944 T allele with severe outcomes in preterm neonatal sepsis.
2. To evaluate the diagnostic performance of predictive models incorporating *OLFM4* genotypes.

3. METHODS

- Study design: Prospective observational cohort study.
- Sample size: used to compare two independent proportions, with α = 0.05 and power = 0.8
  - 23 AA/AG, 40 GG
  - 56 TT/TC, 68 CC


Study population
174 preterm infants with late-onset sepsis included in the study
nSOFA = 0 or nSOFA = 1
Confirmed sepsis (positive blood culture, n = 41)
Suspected sepsis (≥2 clinical symptoms AND ≥2 laboratory tests, n = 133)
OLFM4 genotyping
OLFM4 genotyping (realtime-PCR technique) was performed for SNPs rs17552047 and rs1891944
Cohort by genotypes
OLFM4 rs17552047 genotypes
OLFM4 rs1891944 genotypes
AA/AG n1 = 66
GG n3 = 108
TT/TC n'1 = 88
CC n'3 = 86
Severe outcomes (nSOFA >2)
Followed until severe outcomes (nSOFA >2) or discharge
Sepsis with severe outcomes: nSOFA >2 (n = 39)
Sepsis: nSOFA ≤2 (n = 135)
nSOFA >2
nSOFA ≤2
1
6
32
1
13
25
4
55
76
1
73
61
Statistical analysis
Genotypes distribution between two groups: with severe outcomes and without
Kaplan-Meier analysis to assess risk of severe outcomes of neonatal sepsis
Logistic regression analysis to assess diagnostic performance for prediction of severe outcomes in preterm infants with sepsis

Component	Score				
Respiratory score	**0**	**2**	**4**	**6**	**8**
	Not intubated or intubated, spO_2/fiO_2 ≥300	**Intubated,** spO_2/fiO_2 <300	**Intubated,** spO_2/fiO_2 <200	**Intubated,** spO_2/fiO_2 <150	**Intubated,** spO_2/fiO_2 <100
Cardiovascular score	**0**	**1**	**2**	**3**	**4**
	No inotropes and no systemic corticosteroid treatment	No inotropes and systemic corticosteroid treatment	1 **inotrope** and no systemic corticosteroid treatment	≥2 **inotropes** or 1 inotrope and systemic corticosteroid treatment	≥2 **inotropes** and systemic corticosteroid treatment
Hematologic score	**0**	**1**	**2**	**3**	
	Platelet count ≥150,000/mL	Platelet count 100,000 – 149,000/mL	Platelet count <100,000/mL	Platelet count <50,000/mL	
Total	nSOFA score = Respiratory score + Cardiovascular score + Hematologic score				

Models	Genotypes	
Dominant	(AA+AG) vsGG (TT+TC) vs CC	**One** allele (A, T) was found to influence outcomes, with one or two copies of the allele showing a similar effect
Recessive	AA vs (AG + GG) TT vs (TC + CC)	**Two** allele copies (AA and TT, respectively) exhibited the effect
Additive	AA vs AG với GG TT vs TC với CC	Effects **increased/decreased** in according with **the copies of alles** A/T

4. RESULTS

Table 1. OLFM4 rs17552047 genotypes distribution in neonatal sepsis by severe outcomes

rs17552047	Sepsis *(n = 135)*	Sepsis with severe outcomes (*n* =39)	OR (95% CI)	*p*†
Dominant				
AA/AG, *n* = 66	59 (44%)	7 (18%)	0.28 (0.12–0.68)	**0.005**
GG, *n* = 109	76 (56%)	32 (82%)		
Recessive				
AA, *n* = 5	4 (3%)	1 (3%)	0.86 (0.09–7.94)	0.89
AG/GG, *n* = 169	131 (97%)	38 (97%)		
Additive				
AA, *n* = 5	4 (3%)	1 (3%)	0.35 (0.15–0.78)	**0.01**
AG, *n* = 61	55 (41%)	6 (15%)		
GG, *n* = 108	76 (56%)	32 (82%)		
†Univariate logistic regression				

=> rs17552047 A allele was associated with **reduced risk** of severe outcomes **in both the dominant and additive models**

Table 2. OLFM4 rs1891944 genotypes distribution in neonatal sepsis by severe outcomes

rs1891944	Sepsis *(n = 135)*	Sepsis with severe outcomes (*n* =39)	OR (95% CI)	*p*†
Dominant				
TT/TC, *n* = 88	74 (55%)	14 (36%)	0.46 (0.22–0.96)	**0.04**
CC, *n* = 86	61 (45%)	25 (64%)		
Recessive				
TT, *n* = 2	1 (1%)	1 (3%)	3.53 (0.21–57.71)	0.38
TC/CC, *n* = 172	134 (99%)	38 (97%)		
Additive				
TT, *n* = 2	1 (1%)	1 (3%)	0.52 (0.26–1.06)	0.07
TC, *n* = 86	73 (54%)	13 (33%)		
CC, *n* = 86	61 (45%)	25 (64%)		
†Univariate logistic regression				

=> rs1891944 T allele was associated with **reduced risk** of severe outcomes **in dominant models**

Table 3. Diagnostic performance for predicting severe outcomes in preterm infants with sepsis

Risk factors	Odds ratio	95% CI	*p*
Model 1: Clinical variables			
Birthweight	0.9	0.9 – 1.0	0.01
INR (International normalized ratio)	11.8	3.6 – 39.3	<0.001
Fungal bloodstream infection	35.8	3.4 – 375.9	0.003
Model 2: Genotypes incorporated			
Birthweight	0.9	0.9 – 1.0	0.02
INR	13.8	3.6 – 52.8	<0.001
Fungal bloodstream infection	126.6	8.6 – 1866.6	<0.001
rs17552047 (AA/AG vs GG**)**	0.2	0.1 – 0.6	0.006
rs1891944 (TT/TC vs CC**)**	0.3	0.1 – 0.8	0.017

Initial variables: gender, BW, GA, fever, Gram (+), Gram (-) infection, fungal bloodstream infection, WBC, NEU, PLT, CRP, INR, SNP rs17552047 and rs1891944 genotypes

=> AA/AG and TT/TC genotypes were independent prognostic factors associated with a reduced risk of severe outcomes

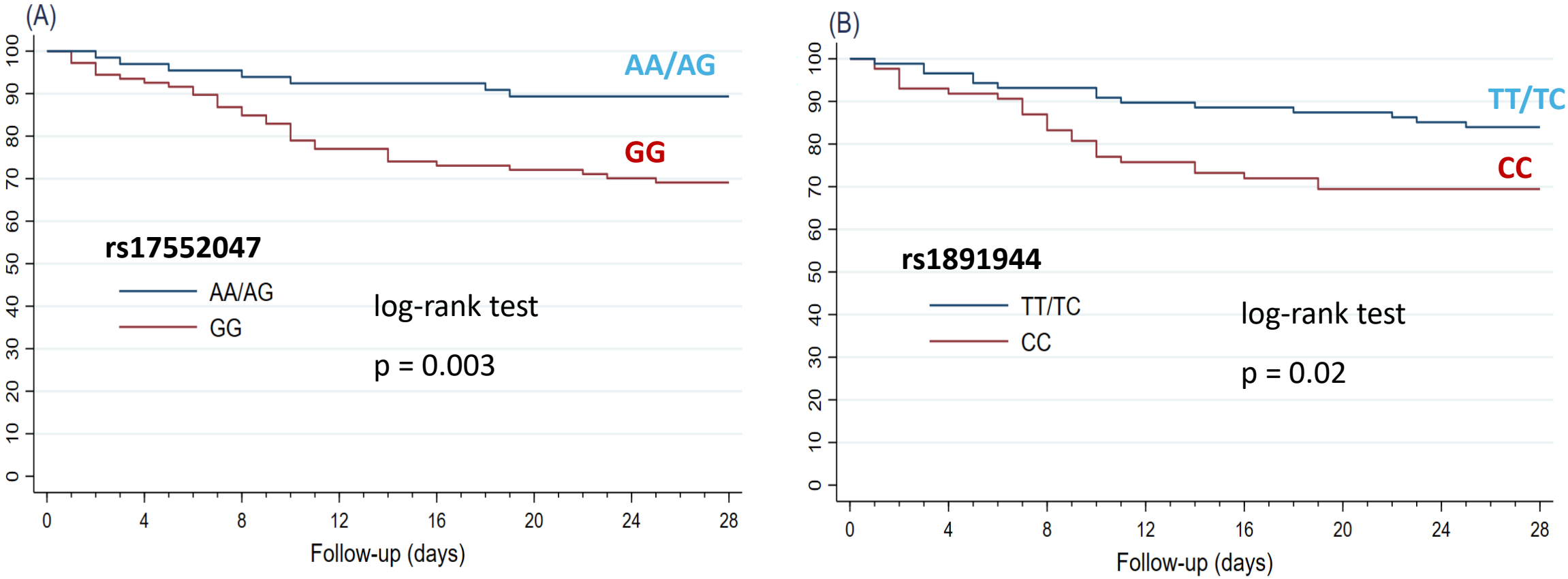


Figure 4. Kaplan–Meier analysis showing the cumulative incidence of severe outcomes in neonatal sepsis, stratified by *OLFM4* polymorphisms in preterm infants. **(A)** *OLFM4* rs17552047: AA/AG (n = 66) and GG (n = 108); **(B)** *OLFM4* rs1891944: TT/TC (*n* = 88) and CC (n = 86)

=> rs17552047 AA/AG and rs1891944 TT/TC genotypes exhibited fewer severe outcomes

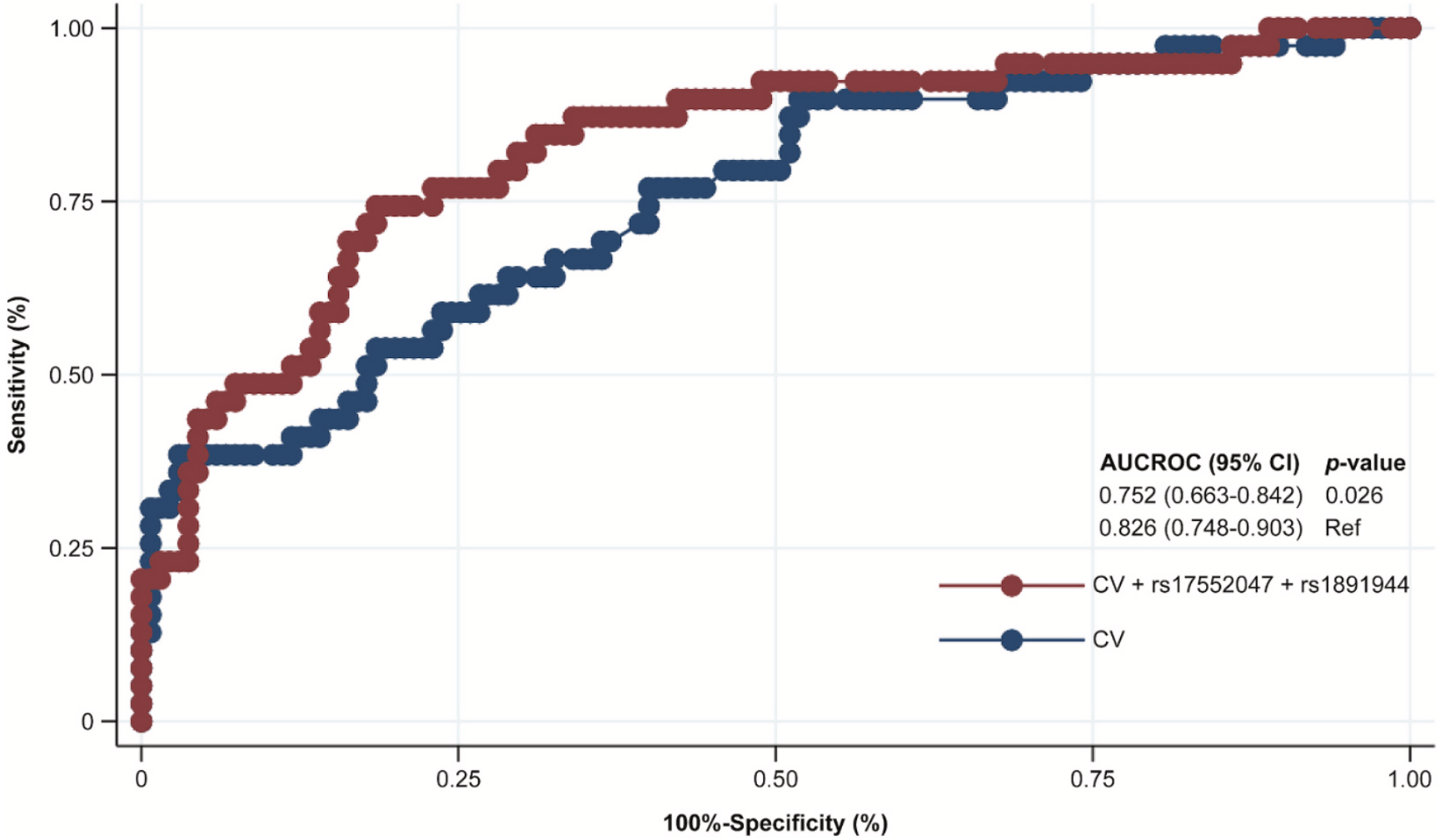


Figure 5. Predictive performance of models for severe outcomes in neonatal sepsis among preterm infants, incorporating *OLFM4* polymorphisms and clinical variables.

=> Genotypes improved the predictive accuracy of the model for severe outcomes (p = 0.03)

5. DISCUSSION & CONCLUSIONS

Our findings support precision-medicine approaches in neonatal sepsis:

- **A allele** (rs17552047) and **T allele** (rs1891944) **consistently** associated with lower risk of severe outcomes, supported by univariate, multivariate, Kaplan–Meier, and Cox analyses.
- Possible **dose-dependent protective effect**: AA → lowest risk; GG → highest risk.
- Including genotypes significantly enhanced predictive accuracy.

Limitations:

- Lack of a universal diagnosis method using blood culture
- Limited number of AA and TT genotypes
- Biological roles of OLFM4: not clear
- Interaction with other genes

Future research:

- Larger, well-characterized cohorts with **microbiologically confirmed sepsis**.
- *In vitro* and *in vivo* investigations to clarify the role of *OLFM4* using a comprehensive **multi-omics approach**.
- **Targeted therapeutic interventions** directed at OLFM4.

THANK YOU!

HCMC, 08/11/2025